On page 31, line 25, delete "liklihood" and substitute --likelihood--.

On page 33, line 8, delete "xenogeneic" and substitute --xenogenic--.

On page 34, line 26, delete "allogeneic" and substitute --allogenic--.

One page 35 line 4, delete "pass" and substitute --passes--; line 18 delete "are effective as carriers" and substitute --is effective as a carrier--.

In the Claims:

1. (Amended) Osteogenic protein expressed from recombinant DNA in a host cell [and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal;], the protein comprising a pair of oxidized subunits disulfide bonded to produce [constituting] a dimeric species,

one of said subunits <u>having an amino acid sequence</u>
<u>sufficiently duplicative of the sequence</u> comprising:



Cont

OPS

Y R D L G G Ρ E Y C E Ε Α Α Y F N M N Α Т N Н Ι V Η F Ι Ε T V Р K P Т L S D K Y C Н

such that the disulfide bonded dimeric species

comprising said subunit has a conformation that is capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal.

2. (Amended) Osteogenic protein expressed from recombinant DNA in a host cell [and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal;], the protein comprising a pair of oxidized subunits disulfide bonded to produce [constituting] a dimeric species,

one of said subunits <u>having an amino acid sequence</u>
<u>sufficiently duplicative of the sequence comprising:</u>

Cont

OP7

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				С	K	K	H	E	L	Y	V	S	F	R	D	L	G	W	eti
		40										50							
Q	D	W I	I	A	P	E	G	Y	Α	Α	Y	Y	C	\mathbf{E}	G	E	С	Α	
-		60										70							
F	P	L N	S	Y	M	N	Α	T	N	Н	Α	I	V	0	T	L	V	Н	
FPLNSYMNATNHAIVQTLV 80 90																			
ਸ	т	N P	F	т	7.7	P	ĸ	P	С	C	Δ	P	т	0	L	N	Α	Т	
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S	V	L Y	F	D	D	S	S	N	V	Ι	L	K	K	Y	R	N	M	V	
120																			
V	R	A C	G	С	Н	•													

such that the disulfide bonded dimeric species

comprising said subunit has a conformation that is capable of

inducing endochondral bone formation in a mammal when disposed

within a matrix implanted in said mammal.

Delete claim 3.

 $\bigcirc \mathcal{A}$

4. (Amended) Osteogenic protein expressed from recombinant DNA in a host cell [and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal;], the protein comprising a pair of oxidized subunits disulfide bonded to produce [constituting] a dimeric species,

one of said subunits <u>having an amino acid sequence</u> sufficiently duplicative of the sequence comprising:

OPP

M Н V R -300 -290 S L R Α Α Α P Н S F Α \mathbf{L} WA P L F L \mathbf{L} -270 -280 L D F L D N E V Н S S F Ι Н R R -260 -250 L R S Q Ε R R \mathbf{E} М Q R Ε I L S Ι \mathbf{L} G \mathbf{L} R -230-240P R P Н \mathbf{R} P L Q G K Η N S A P М F M \mathbf{L} Н -220 -210 E E G G G P G G F S L Y N A М V G Q D Α -190 -200 Y P Y K A V F S T Q G P P L A S Q D S L -170 -180F \mathbf{v} S F \mathbf{v} N L V E Н D K Η \mathbf{L} T D Α D М M -160 -150 F F F D S P F H P Y R E R \mathbf{L} K Ι E R Н Н -140-130G F R Ι K D \mathbf{E} R E E A V Т Α E Y Y Ι R Α -120 -110E T S V Y Q V G R F D N F R Ι L Q E Η L -90 -100 S D S R T \mathbf{L} W A S G L E L F L \mathbf{L} D E E W -80-70 V F D Ι T Α T S N W v V N P N L G H R Η -60-50L Q L S V E T D G Q S N P K A G L L Ι L -40 -30 G F V Ι R Н G P N K Q P M Α F F K Α Т -20-10E V Н F S S T K Q R S S R Ι R G Q N R 1 10 T P K E R N K N A L М A Α N S S S Ε *] * 20 30 C V D Q R Q Α K E L Y S F R G D L W 50 40 Y C Q D W Ι Ι A P E G Y Α Y E G \mathbf{E} C Α 60 70 F P T Α V L N S Y N N Н I Т V Н М Α Q L 80 90 P C C F Ι N P E T V K A ₽ T Q L N Α Ι

Opt.

() Dix

100 S V L Y F D D S S N V I L K K Y R N M V 120 V R A C G C H

wherein the underlined residues indicate a potential cleavage site for an N-terminal secretion signal peptide [and the starred residues indicate a potential cleavage site for protein maturation], such that the disulfide bonded dimeric species comprising said subunit has a conformation that is capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal.

Claim 5, line 1, delete "3,".

Claim 5 / line 2, delete "an apparent" and substitute --a--.

Claim 6, lines 2 and 3, each occurrance, delete "an apparent" and substitute --a--.

Claim 7, line 1, delete "3,".

Claim 8, line 2, delete "an apparent" and substitute --a--.

Claim 9, lines 2 and 3, each occurrence, delete "an apparent" and substitute --a--.

Claim 10, line 1, delete "3,".

Claim 11, line 1, delete "3,"

12. (Amended) The invention of claim 1, 2, [3,] or 4 wherein the other subunit comprises the amino acid sequence:

 $[\phi_{PM}]$ -10K K QEA 20 H R Q Α K K I A P Y D Ι \mathbf{E} C E Α S Ρ N Y M N N Α V Н 80 90 Ι P N E Р C Ι 100 D S S N V D Ι L K Y K Y R G C Н A C

[wherein the standard desidues are optional].

13. (Amended) The invention of claim 1, 2, [3], or 4 wherein the other subunit comprises the amino acid sequence:

OP Н V R М -300 -290 S L R Α Α A P Н S F L Α P L L Α L -280 -270R D F S L D N E V Н S S R Α L F Ι Н -260-250R L \mathbf{R} S E \mathbf{R} \mathbf{R} E М Q R E L S G L Q Ι Ι L -240-230 P Н R Ρ P Н Q G K Η R L N S Α P М F M L -220-210 D L Y N M Α V E E G G G Р G G F S Α G Q -200 -190Y P Y K Α F S G P L Α S L Q D S -180-170F T M S F Н L D Α D М V N L V E Н D K -160-150F н R E Ε F F Н P R Y H R F D L S K Ι P -140-130 E G T Ι E Α Α R Y K Y I E A V D R R -120-110 F D N E T F \mathbf{R} Ι V Y Q V Q Н L G R -100 -90 E S D L F L L D R \mathbf{L} W Α S E \mathbf{E} G W \mathbf{L} -80-70 V F S Н V D Ι Т Α Т W V N P R Η N L G -60-50 L Q \mathbf{L} S E T \mathbf{L} D/ G V Q S Ι N P K L Α G \mathbf{L} -40 -30 Ι G R H G Q N K Q P F M V A F F K Α T -20-10 E V \mathbf{F} S I R R S Т G K Q \mathbf{R} S S N R 1 10 K Т P K N E A R Q \mathbf{L} M Α N V Α E N S S S *] 20 30 D Q Α C K Η E L Y V S F R D L G W 40 50 Q D Ι Ι P Æ G Y Α Y Y C Α Α E G E Α 60 70 F P N S Н Y M N T N Α Ι V Q T L V Н

Const

(Jong)

80
F I N P E T V P K P C C A P T Q L N A I 100
S V L Y F D D S S N V I L K K Y R N M V 120
V R A C G C H

wherein the underlined residues indicate a potential cleavage site for an N-terminal secretion signal peptide [and the starred residues indicate a potential cleavage site for protein maturation].

Claims 14-19 line 1 of each claim, delete "3,".

Claim 17, 18/and 19, last line of each, delete "*".

Delete claims 20 and 22-27, pursuant to the requirement for restriction, without prejudice.

Ad

21. (Amended) [The] A protein expressed from [the DNA of claim 20] a DNA sequence encoding an amino acid sequence sufficiently duplicative of that of the sequence encoded by the gene of Figure 1B such that said encoded sequence induces bone or cartilage formation in dimeric form when implanted in a mammal in association with a matrix.